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Original Communication
Alcohol drinking and risk of non-Hodgkin's lymphoma

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Objective: To analyse the relation between alcohol intake and the risk of non-Hodgkin's lymphoma (NHL).
Design: Hospital-based case–control study.
Settings: The greater Milan area and the province of Pordenone, Northern Italy.
Subjects: Cases were 446 (256 men and 190 women) with histologically confirmed incident NHL, and controls were 1295 (791 men and 504 women) with acute non-neoplastic conditions.
Results: Compared to non-drinkers, the odds ratio (OR) was 0.92 for < 3 drinks per day, 0.98 for 3–6 drinks, and 1.02 for ≥ 7 drinks per day. Wine drinking was also not associated with risk, and the OR was 0.85 for drinkers of ≥ 7 drinks/day compared to non-drinkers. Beer and spirit intake was also not associated with NHL risk.
Conclusions: Our study, based on a population with relatively high alcohol intakes, indicates that there is no appreciable association between intake of various alcoholic beverages and the risk of NHL.
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Descriptors: non-Hodgkin's lymphoma; alcohol intake; risk factors; case–control study
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Introduction

Epidemiological evidence on the relation between alcohol intake and the risk of non-Hodgkin's lymphoma (NHL) is scanty and controversial. A cohort study, evaluating the relation between alcohol intake and lymphohematopoietic neoplasms of Japanese men living in Hawaii and based on 36 cases of NHL, found increased risks of these neoplasms in association with total alcohol and, specifically, with beer intake (Kato *et al*, 1992). Conversely, in the Iowa Women's Health Study cohort (Chiu *et al*, 1999), an inverse association with total alcohol intake was found, not attributable to one particular type of alcohol-containing beverage, although intake of red and white wine showed the strongest protective effect.

Case–control studies showed inconsistent results too, since one found a direct association (De Stefani *et al*, 1998), and others reported no (Cartwright *et al*, 1988; Brown *et al*, 1992) or inverse associations (Nelson *et al*, 1997).

Given the widespread interest in the beneficial effects of moderate alcohol intake on several diseases, we updated and re-analysed in more detail data on alcohol intake from a case–control study of NHL on a population with high levels of alcohol drinking (La Vecchia, 1995).

Subjects and methods

Data were derived from a case–control study of lymphoid neoplasms and soft tissue sarcomas, conducted between 1981 and 1994 in the greater Milan area and the province of Pordenone, Northern Italy (Franceschi *et al*, 1989; Tavani *et al*, 1997).

The updated dataset included 446 (256 men and 190 women, median age 58 y, range 17–79) histologically confirmed cases of incident NHL (ICD-9 200 and 202). Controls were 1295 subjects (791 men and 504 women, median age 57 y, range 17–79), admitted to hospital for a wide range of acute, non-neoplastic diseases. Of the comparison group, 15% were admitted for non-alcohol-related traumas, 27% for other orthopedic disorders, 29% for surgical conditions, and 28% for other miscellaneous illnesses (such as ear, nose and throat, eye, dental or skin disorders). All admission diagnoses known to be related to long-term modifications in diet, cigarette smoking or alcohol drinking were excluded from the control group. On average, less than 3% of the eligible subjects (cases and

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controls) refused to be interviewed. Interviews were conducted during hospital stay for both cases and controls; cases were interviewed during the admission to hospital for diagnosis establishment.

Trained interviewers used a structured questionnaire to collect data on socio-demographic characteristics, anthropometric measures, history of selected medical conditions, selected occupational exposures, smoking status, alcohol drinking and intake of coffee and of 14 selected food items. Information on alcohol referred to the year prior to diagnosis and included the number of days per week, the number of drinks per day for each type of alcoholic beverage (wine, beer, spirits), and the duration of the habit in years. The average number of all alcoholic drinks per day was computed as an indicator of total alcohol consumption (one drink corresponded to approximately 150 ml of wine, or 330 ml of beer, or 30 ml of spirits, corresponding to 12–15 g of ethanol).

Odds ratios (OR), and the corresponding 95% confidence intervals (CI), were derived by multiple logistic regression equations, including terms for centre, age, sex, education, marital status, blood transfusions, diabetes and intake of milk, meat, green vegetables and fruit.

Results

Table 1 considers selected measurements of alcohol drinking. With reference to total alcohol consumption, compared to non-drinkers, the multivariate OR was 0.92 for < 3 drinks per day, 0.98 for 3–6 drinks, and 1.02 for ≥ 7 drinks per day. Similarly, wine drinking, which in this population accounts for over 80% of total alcohol consumption (La Vecchia, 1995), was not associated with NHL risk: compared to wine non-drinkers, the OR was 0.78 for drinkers of < 3 drinks of wine per day, 0.84 for drinkers of 3–6 drinks, and 0.85 for drinkers of ≥ 7 drinks of wine per day. Further adjustment for smoking and occupational exposures did not materially modify the risk estimates. Beer and spirit intake was also not associated to NHL risk, the OR being respectively 1.17 and 1.55 for drinking of ≥ 3 drinks per day. None of the trends in risk was significant.

When the analysis was restricted to women, compared to non-drinkers (55 cases and 141 controls), the OR was 0.82 (based on 101 cases) for < 3 drinks per day, and 0.75 (based on 33 cases) for ≥ 3, with no significant trend in risk. Corresponding values for wine intake were 0.88 (based on 107 cases) and 0.67 (non-significant, based on 23 cases), with again no significant trend in risk.

Table 1 Distribution of 446 cases of non-Hodgkin's lymphoma (NHL) and 1295 controls and corresponding odds ratios with 95% confidence intervals (CI), according to alcohol drinking. Italy, 1981–1994

	NHL		*Controls*		
	n	%	n	%	*Odds ratios (95% CI)*[a]
Total alcohol intake (drinks/day)[b]					
Non-drinkers	68	15.3	215	16.7	1[c]
< 3	155	34.9	481	37.3	0.92 (0.65–1.30)
3–6	135	30.4	381	29.5	0.98 (0.66–1.45)
≥ 7	86	19.4	214	16.6	1.02 (0.64–1.63)
χ^2, trend					$P = 0.84$
Wine intake (drinks/day)[b]					
Non-drinkers	85	19.1	245	19.0	1[c]
< 3	165	37.0	516	39.9	0.78 (0.56–1.08)
3–6	141	31.6	389	30.1	0.84 (0.58–1.24)
≥ 7	55	12.3	142	11.0	0.85 (0.52–1.39)
χ^2, trend					$P = 0.59$
Beer intake (drinks/day)[b]					
Non-drinkers	320	71.9	964	74.5	1[c]
< 1	54	12.1	177	13.7	0.96 (0.67–1.36)
1–2	39	8.8	78	6.0	1.47 (0.96–2.27)
≥ 3	32	7.2	75	5.8	1.17 (0.73–1.87)
χ^2, trend					$P = 0.21$
Spirits intake (drinks/day)[b]					
Non-drinkers	313	70.3	956	73.8	1[c]
< 1	52	11.7	182	14.1	0.86 (0.61–1.23)
1–2	65	14.6	130	10.0	1.40 (0.99–1.99)
≥ 3	15	3.4	27	2.1	1.55 (0.79–3.05)
χ^2, trend					$P = 0.08$

[a]Estimates from multiple logistic regression equations including terms for centre, age, sex, education, marital status, blood transfusions, diabetes and intake of milk, meat, green vegetables and fruit.
[b]The sum does not add up to the total because of some missing values.
[c]Reference category.

Discussion

Our study, based on a population with substantially high alcohol intake, confirms that there is no appreciable association between moderate or heavy intake of various alcoholic beverages and the risk of NHL.

This study was hospital-based and may be open to criticism, since drinking may be related to several conditions requiring hospital admission (La Vecchia *et al* 1995); thus, the use of hospital controls may overestimate the level of drinking in the reference group. However, we carefully excluded from the control group patients admitted for chronic conditions, particularly those related to alcohol intake, smoking, diet and alcohol-related traumas: thus, only acute conditions, unrelated to recognised risk factors for NHL, were included. The results were consistent when separate analysis by major diagnostic categories of controls was made. Interviews were conducted in hospital for cases and controls, participation was almost complete, cases and controls were drawn from the same catchment areas, and adjustment for a number of potentially relevant covariates did not appreciably modify any of the risk estimates. Alcohol drinking and/or NHL may be related to cigarette smoking, to a poorer diet, occupational exposure or other risk factors (La Vecchia *et al*, 1987, 1989, 1992; Tavani *et al*, 1994; D'Avanzo *et al* 1997). This, however, may apply less to Italy, where alcohol drinking is widespread (La Vecchia *et al*, 1995). Information on alcohol drinking was satisfactorily reproducible, as the Pearson correlation

coefficient between two interviews of the same subjects about 6 months apart was 0.81 for consumption of any type of alcohol (D'Avanzo *et al*, 1996). Thus, it is unlikely that the present results are substantially influenced by selection, information bias or confounding.

Our findings do not support those of the Iowa Women's Health Study (Chiu *et al*, 1999), since also when the analysis was restricted to women, no significant association and no trend in risk were found for either total alcohol or wine intake. Moreover, as over 80% of this Italian population drunk wine frequently and in considerable amounts, our data support no appreciable association between NHL and wine drinking. No separate information on red and white wine was available, as in Italy they tend to be both drunk by the same subjects depending on the type of food eaten.

The present data are consistent with the general evidence on the issue, since of two cohort studies one found a direct (Kato *et al*, 1992) and one an inverse association (Chiu *et al*, 1999), and of four case–control studies one found a direct (De Stefani *et al*, 1998), one an inverse (Nelson *et al*, 1997) and two no appreciable association (Cartwright *et al*, 1988; Brown *et al*, 1992). Thus, they provide convincing evidence that alcohol drinking—mainly wine, even in relatively high amounts—is not appreciably related to the risk of lymphoid neoplasms.

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